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REVIEW OF THE CASEBackground and History

Through Dr. Jacobson of Harvard University, the mushroom "Teonanactl" of the Aztecs was brought to our attention as having CNS stimulant effects. Although the literature cited this to be Panaeolus campanulatus, it has been learned that a larger one, Psilocybe is the mushroom responsible for the stimulant and hallucinogenic action. Samples of Panaeolus and another unidentified CNS stimulating mushroom were sent to us by Mr. Paracides-Kinson via Mr. John Klopfer, Mexico. The Panaeolus showed no appreciable activity, but the unidentified material was classified as Psilocybe cubensis which is the one the Wassons claim is used for stimulation by the Indians. Discussions have been held with Dr. Gordon Wasson who has published the results of his expeditions in search of the hallucinogenic mushrooms. At present, Dr. Moore of the University of Delaware, a contact of ours as well as one of the group with Mr. Wasson, is working on extracts of Psilocybe for us.

Extraction of the dried ground mushrooms with 100% ethanol at room temperature followed by concentration in vacuo at temperatures below 35°, extraction with hexane, and finally lyophilization yields approximately 1/2% of water-soluble mucous solid (MW 770), giving trace alkaloid tests with Mayer's reagent.

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purpose of this report is to report the results of Psilocybe saurolescens,
specimen 4771, on the behavior of the test animals. The purpose of this report is to report the effect in animals. The following is a report of our findings:

↓ ACTIVITY
↑ INTEREST

In the nonbutylscopolamine, blood pressure, carotid pressure responses following primary dose of 0.1 to 0.5 mg. A good dose response effect ~~was~~ observed. Atrial ~~arrhythmia~~ arrhythmia was observed in one experiment at high dose levels, it appears that S.F. No. 677^a failed to have a significant effect on the autonomic nervous system. It may be interesting to note here that Haloperidol differs from Mescaline or LSD in that the latter two substances are parasympathetic agents in the anesthetized rat and clinically Naloxone; Sclman.

14. Administrative: Will not affect or prevent or alter FTO seizures in any other way as shown in 13 and 14.

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... of December 9, 1957 on

...

...

... Effect of SKB dissolved in Rats (D.O. & I.P.)

LOW-TRONCH
ESCAPE
RESPONSE

4. Dose Response in Rats (D.O. & I.P.)

In dose doses of 25 or 50 mg/Kg failed to produce significant behavioral changes. At a dose of 10 mg/Kg, apprehension, panting, mydriasis and stimulation were noted. At the 25 mg/Kg level, restlessness, vocalizations, mydriasis, and apprehension were evident. Our impressions in this study were largely subjective. No obvious changes in behavior were apparent although at times the observers thought that slight behavioral changes were noted; however, these equivocal effects indicate that our recorded observations may be questioned. In the monkeys, intravenous doses of 25 or 50 mg/Kg failed to produce behavioral changes or significant side effects. It should be mentioned here that this sample of SKB No. 6778 had been in the laboratory for four months and may have lost potency.

Overall Summary:

It is apparent from the data presented that we were not able to demonstrate any unusual pharmacologic activity after administration to rats and mice. SKB No. 6778 failed to antagonize 'chlorazine' (in contrast to LSD) and did not induce any characteristic effects such as those seen after administration of chlorazine (scratch phenomenon).

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Psychic Effects of Psilocybe cubensis in Dogs and Monkeys

Table I

1 - Dogs

Dose (mg/Kg)

Observations

10

myriasm, salivation, panting, apprehension

25

myriasm, crying, vocalizing, slight salivation, apprehension, no effect on appetite.

2 - Monkeys

Dose (mg/Kg)

Observations

25

no side effects

50

Deep increased respiration on injection, mouth movement

B. Psilocybe cubensis - Sample No. 2 submitted to E. Macko on 2/11/58 by Dr. I. Pachter

1. Dose Range in Dogs

Intravenous doses of 25, 50 or 75 mg/Kg were administered to each of three dogs respectively. After injection all of the dogs exhibited side reactions; however, whether these reactions are indicative of behavior changes could not be determined with certainty. At the 25 mg/Kg level, panting, salivation, myriasm, apprehension and apprehension, jaw movement and all oral cavities were observed. In addition, this animal sat quietly, frequently exhibiting a posture (head to 1.0 x/min), raised his head toward the ceiling and appeared to be looking for something. This behavior continued for three hours following injection. A dose of 50 mg/Kg was administered to the animal 10 minutes following

subject was then observed and was very quiet for a five hour observation period. A dose of 75 mg/Kg produced salivation, diarrhea, ataxia, stiff-leggedness, dilated pupils, jaw movement, apprehension, body shakes and an initial transient stimulation. Further, this dog appeared to be looking for something and stood facing the back of the cage for three to four hours.

In these animals, SKF No. 6773 produced visible biological side effects following doses of 25 to 75 mg/Kg, intravenously.

One can only speculate about the connection of these effects and the hallucinogenic effects reported in man.

Table II

Interactions of the 30 mg/kg Dose on JFF No. 4778 (normal No. 2)

Dose: 35 mg/kg

Timid Collie

Time of Admin. 9:00 A.M.

Wt. 12.6 Kg.

Observations:

panting, inc. resp. (2)

10:05 - panting, jaw movement, slight salivation, dil. pupils

10:15 - sitting quietly in corner, panting and extruding and pulling in tongue very rapidly, lifting head in circular motion to the right as seen in 'Compazine'. Jaw movement 80 x/minute

10:30 - sitting quietly, doring as if sedated, closing eyes, head has tendency to droop.

11:00 - jaw movement, rapid resp., tongue movement, raising head to right, can be interrupted

11:30 - as above, rapid resp., panting

3:00 - normal

4/12/68 all data normal

Dose: 50 mg/kg

Friendly Black

Time of Admin. 9:45 A.M.

Wt. 10.4 Kg.

salivation (sl) (2)
myriasis (3)
vocalizing (sl) (3)
lying down (deact ?) (4)

10:05 - emesis, depressed, dil. pupils

10:20 - laying down, eyes open, depressed

11:00 - depressed, apprehensive

11:30 - depressed

3:00 - depressed

75 mg/kg

Timid Beagle

Time of Admin. 9:45 A.M.

Wt. 8.7 Kg.

salivation (1)
diarrhea
ataxic
stiff legged
jaw motion (3)

10:05 - dil. pupils, jaw movement, salivation, tense, sl. shakes

10:15 Standing facing back of cage, very apprehensive, sl. salivation, sl. ataxia as if afraid to move, dilated pupils. Looking about cage as though hunting for something

10:20 - laying down, eyes open, rational and able to respond to handling and stimuli.

11:00 - sl. salivation, jaw movement, dil. pupils, attentive, blinking eyes, can be interrupted

11:30 - as above

3:00 - apprehensive

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2. Daily Administration of SKF No. 6778 (Sample No. 2) in Dogs and Monkeys

In order to attempt to produce more definitive hallucinogenic or biological activity, daily administration of SKF No. 6778 was initiated in dogs and monkeys for five days with the following dose schedule.

Species	Days. Dose (mg/Kg)				
	1	2	3	4	5
Dog 2,3,5	25 (i.v.)	→	50 (i.v.)	200 (i.v.)	800 (oral)
Dog 4, 6	100 (oral)	→	200 (oral)	800 (oral)	"
Monkey 28, 43	25 (i.v.)	→	50 (i.v.)	200 (i.v.)	"

Our data is summarized in Table III.

Results:

No significant changes in the behavior of the monkeys was observed from daily doses of 25 to 200 mg/Kg of SKF No. 6778, intravenously, for four days followed by one dose of 800 mg/Kg, orally, on the fifth day.

In the dogs, questionable behavioral changes were observed in some of the animals (Dogs No. 5, 6) in doses below 200 mg/Kg, intravenously. However, doses of 200 mg/Kg, intravenously or 800 mg/Kg, orally, produced considerable side effects which were characterized by ataxia, crying, apprehension, tremors, mydriasis, etc. As shown in Chart III, it appeared to the observer that the side effects after 800 mg/Kg, orally, were more intense than those following 200 mg/Kg, intravenously. Therefore, on the fifth and last day all of the animals received 800 mg/Kg of SKF No. 6778, orally. In the dogs, emesis as well as significant behavioral changes and side effects were observed. At gross observation, autopsy of 2 of the dogs 4 days after the last treatment failed to disclose tissue damage.

Table III

Daily Administration of Psilocybe cheruleum in Dogs and Monkeys

Dose	600 mg/kg				600 mg/kg
	1	2	3	4	5
100 mg/kg (i.v.)	Side effects: intermittent and intense crying	slight salivation	No side effects	sl. salivation after injection, slight dyspnea, ataxia for 3 hrs., normal in 6 hrs.	erectile post. of penis for 10 min. mild tremor
25 mg/kg (i.v.)	No side effects	No side effects	No side effects	ataxia, apprehension, covering in corner, crying, excited, dyspnea apprehension > 6 hours	erectile post. of penis for 10 min.
100 mg/kg (p.o.)	barking, crying, very excited, spasms, panting, jumps to one side of cage for 12 min. crying for 10 min.	barking, vocalizing, very excited when approached can be calmed down	barking, vocalizing, excited	barking, excited	Very friendly, jumps around, only slightly apprehensive
100 mg/kg (p.o.)	No effects	No effects	No effects	crying, vocalizing for 1 hr., dyspnea, depressed > 1 hr.	friendly, hyperactive

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		1		2		3		4		5		Observations before Dose 1	
		Dose: 100 mg/Kg (p.o.)		100 mg/ Kg p.o.		200 mg/ (p.o.)		800 mg/Kg (p.o.)		800 mg/Kg (p.o.)			
1	1	Healthy, crying, panting		no effects		crying, whining, can be interrupted		panting, muscle ripple or spasm on thigh tremors crying 15 min. holding 1 hr. depressed 3 hrs. normal 6 hrs.		vomited part of capsule in 20 min. depressed 1 hr., normal in 3 hrs.		Very friendly tries to escape is scared, nervous active	
	23	Dose: 25 mg/Kg (i.v.) deep respiration on injection transient drooping of eyelids, mouth movements 2 1/2 hrs.		25 mg/Kg (i.v.) deep respiration on injection		50 mg/Kg deep resp. on injection mouth movements 5-10 min.		200 mg/Kg (i.v.) deep resp. on injection mouth movements apprehensive, tremors, head movements		800 mg/Kg (p.o.) mouth movement (?)		Very aggressive	
	13	deep respiration on injection transient droop of eyelids		deep resp. on injection		deep resp. on injection		deep respiration on injection		mouth movement (?)		Very aggressive	

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Conclusion:

Psilocybe caerulescens produced side effects and some behavioral changes in dogs following massive doses of 25 to 200 mg/kg intravenously or 100 to 800 mg/kg, orally. Although our observations are purely subjective and can lead only to speculation concerning the hallucinatory effect of this substance in man, we have established that Psilocybe caerulescens should be relatively non-toxic.